REMARKS

This amendment is responsive to the Office Action mailed September 19, 2007. Applicants submit concurrently herewith: (1) a substitute specification, including a marked version containing markings showing all changes made and a clean version; (2) a Supplemental Information Disclosure Statement with references CA-CB; and (3) a Petition for Extension of Time.

The specification as originally filed does not contain sequence identifier for each sequence disclosed in the specification. Applicants submit herewith a substitute specification in which assigned SEQ ID NOs have been included to identify each of the disclosed sequences. Pursuant to 37 C.F.R. § 1.125, a marked version of the substitute specification with markings showing all changes relative to the specification as filed and a clean version of the substitute specification are submitted. The substitute specification contains no new matter. Applicants respectfully request that the originally filed specification be replaced with the substitute specification submitted herewith.

Claims 1-13 were pending in the application. In the Office Action mailed September 19, 2007, claims 1-13 have been rejected. In the instant Amendment, claims 1, 10 and 11 have been amended, and claims 14-24 have been added. Upon entry of the instant Amendment, claims 1-24 will be pending in the application.

Claim 1 has been amended to recite that the composition does not comprise any OFA epitope that specifically stimulates T suppressor cells. Support for the amendment is found in the specification at page 13, lines 11-13; page 14, lines 17-20; and page 15, lines 27-30.

Claims 10 and 11 have been amended to correct a grammatical error.

Claims 14-24 have been added. Support for claim 14 is found in the specification, *e.g.*, at page 33, lines 5-9. Support for claims 15-18 is found in the specification, *e.g.*, at page 33, line 17 through page 34. Support for claim 19 is found in the specification at page 22, lines 20-25. Support for claims 22-23 is found in the specification, *e.g.*, in Table 2 at page 54-55. Support for claim 22 is found in the specification, *e.g.*, at pages 13-14. Support for claims 23-24 is found in the specification, *e.g.*, at pages 15-16.

No new matter has been added by these amendments. Thus, entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

THE OBJECTION TO THE SPECIFICATION

The specification has been objected to for failing to use assigned sequence identifiers in all instances where the specification refers to a sequence. Applicants have submitted herewith a substitute specification in which assigned SEQ ID NOs have been included such that each sequence disclosed in the specification is identified by its assigned sequence identifier. The objection is therefore obviated.

THE REJECTION UNDER 35 U.S.C. § 112, Second Paragraph

Claim 11 has been rejected under 35 U.S.C. § 112, second paragraph, on the ground that the recitation "wherein said at least one OFA epitope," lacks sufficient antecedent basis. Applicants have amended claim 11 to depend on claim 10. The rejection is therefore obviated.

THE REJECTION UNDER 35 U.S.C. § 112, First Paragraph

Claims 1-13 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully disagree with the Examiner for reasons set forth below.

At the outset, Applicants respectfully submit that claims 12-13 are directed to a method for preparing an

immunotherapeutic composition. The Examiner's reasoning does not appear to be relevant to these claims. Nonetheless, Applicants respectfully submit that detailed description of the claimed method is found in the specification at, *e.g.*, page 26, line 16 through page 29, line 17.

Contrary to the Examiner's contention, the specification of the present application does not merely disclose OFA epitopes by their functions. The specification provides a detailed description of not only the general structural characteristics but also the structures, *i.e.*, amino acid sequences, of specific OFA epitopes embraced by the claims. In this regard, the specification describes the complete structure of the OFA at page 19, line 16 through page 20, line 52. The specification also describes the regions of OFA where the epitopes are contained, *e.g.*, N-terminal or C-terminal region for epitopes that specifically stimulate proliferation of clones of Tc cells (see, the specification at page 22, line 30 through page 24, line 9). The paragraph also discloses specific epitopes by their amino acid sequences (see, *e.g.*, Table 2 at pages 54-55 of the specification). Numerous epitopes are disclosed at pages 23-25.

Therefore, the present application is distinguishable from both *Regent's of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 2004) and *University of Rochester v. G.D. Searle Co.*, 358 F.3d 916 (Fed. Cir. 2004). In each of these cases, there are no descriptions of the structure of a single embodiment of the claimed composition *in the specification* (emphasis added). There are only disclosures of a general plan and/or experimental procedure to obtain the claimed composition. In contrast, the present specification provides a detailed description of not only the general structural and functional characteristics but also the specific structures, *i.e.*, amino acid sequences, of claimed OFA epitopes.

The Examiner also contends that the present application does not adequately describe, with the requisite degree of particularity necessary to satisfy the written description requirement of the genus of OFA epitopes that satisfy the functional limitation of eliciting a CTL, and that in order to satisfy the written description requirement, for a genus claim, Applicants must include sufficient description of at least a representative number of species by actual reduction to practice. The Examiner alleges that Applicants have not disclosed an actual reduction to practice. That is clearly not the case.

Applicants respectfully submit that the present application claims epitopes contained in a 295 aa protein, *i.e.*, the OFA or iLRP. Applicants have examined the entire sequence of the OFA protein to identify epitopes that are specifically stimulate Tc, Ts, or Th cells. For example, Table 2 at pages 54-55 lists epitopes that stimulate each of the three different types of lymphocytes across the length of the OFA protein. Detailed descriptions of epitopes in different aa regions are also presented in the specification, *e.g.*, at page 57, line 7 through page 60, line 13 for epitopes in aa region 62-135; at page 60, line 14 through page 63, line 23 for epitopes in aa region 136-166; at page 63, line 24 through page 66, line 6 for epitopes in aa region 168-242; and at page 66, line 7 through page 68, line 24 for epitopes in aa region 243-295. Although the analysis was carried out using mouse as the example, the sequence of the OFA is highly conserved between mouse and human (see, the specification at page 19, lines 28-35). Applicants have shown that the results obtained from mouse are also applicable to at least human (see, e.g., the specification at page 26, lines 5-16 and page 69, line 1 through page 76, line 17). The Office action does not contain any explanation as to why the large number of OFA Tc and Th epitopes disclosed in the specification is not representative and

supportive of the claimed genus, from the standpoint of § 112, first paragraph (written description).

Therefore, the present application is distinguishable from *Noelle v. Lederman*, 1355 F.3d 1343 (Fed. Cir. 2004). In *Noelle*, the court found that *Noelle* did not provide sufficient support for the claims to the human CD40CR antibody because *Noelle* failed to disclose any structure of human CD40CR antibody or antigen. In contrast, in the present application, structures (*i.e.*, aa sequences) of epitopes that stimulate each of the three different types of lymphocytes across the length of the OFA protein are identified and disclosed.

Therefore, Applicants respectfully submit that claims 1-13 (as well as new claims 14-24) fully comply with the written description requirement. The rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 103

Claims 1-13 have been rejected under 35 U.S.C. § 103(a), as being unpatentable over Irie *et al.*, 1979, J. Natl. Cancer Inst. 63(2):367-373 ("*Irie*") or Rohrer *et al.*, 1999, J. Immunol. 162(11):6880-6892 ("*Rohrer*") in view of Fikes *et al.*, U.S. Patent 6,602,510 ("*Fikes*") and Oseroff *et al.* 1999, Vaccine 16(8):823-833 ("*Oseroff*"). Applicants respectfully disagree with the Examiner for reasons set forth below.

Rohrer teaches that breast cancer patients produce clonable T lymphocytes specific for OFA. However, *Rohrer* was peripheral blood T cells and cultured them with autologous tumor to induce proliferation of the T cell able to recognize antigens presented by the tumor cells *in vitro*. About 32% of the tumor-reactive T cells from all patients tested were specific for OFA/iLRP. *Rohrer* does not teach or suggest that OFA contains separate epitopes that specifically stimulate T cytotoxic lymphocytes, T suppressor cells, or T helper lymphocytes, respectively. Nor does *Rohrer* teach or suggest utilizing

epitopes that specifically stimulate T cytotoxic lymphocytes and/or T helper lymphocytes in a composition without epitopes that specifically stimulate T suppressor cells.

In fact, a teaching that OFA may stimulate T cytotoxic lymphocytes would not have led a person skilled in the art to the presently claimed invention. As explained in the specification (at page 12, line 23 through page 13, line 8), OFA/iLRP-specific Tc and Ts cells are both CD8 T cells and, with the exception of the spectrum of cytokines that they produce, their functional abilities are basically the same. It has been demonstrated that the relative stimulation of Tc and Ts cells by OFA/iLRP in mice is dose-dependent; since Ts cells have lower affinity T cell antigen receptors (TCRs) compared to TCRs on Tc cells, Tc cells respond to significantly smaller doses of OFA/iLRP than Ts cells. These observations suggested that dosage amount (as opposed to the epitope itself) is an important variable in potentiating an immune response without stimulating Ts cells. On the basis of these facts and observations, Applicants submit that a person skilled in the art would have expected Tc and Ts cells to be reactive to the same spectrum of OFA epitopes, and would not have expected that the OFA protein contains separate epitopes that specifically stimulate T cytotoxic lymphocytes, T suppressor cells, or T helper lymphocytes, respectively.

Regarding *Irie*, although termed an OFA antigen, the OFA antigen of *Irie* is a totally different antigen than the OFA of the present invention. The OFA of the present invention is immature laminin receptor protein, while the OFA of *Irie* is ganglioside GM2 (see, *e.g.*, Tai, *et al.*, 1983, "Ganglioside GM2 is a human tumor antigen (OFA-I-1)" Proc. Natl. Acad. Sci. (USA) 80:5392-5396, a copy of which is submitted in the Supplemental Information Disclosure Statement as Reference CB). It can be seen that *Irie*'s OFA is not even a protein, but a glycolipid.

In addition, *Irie* teaches only inducing antibody responses, not T lymphocyte immunity.

Neither *Fikes* nor *Osteroff* is concerned with OFA antigen epitopes. *Fikes* teaches using epitopes of several different tumor proteins (p53, MAGE2, MAGE3, Her2/neu, and CEA) for use in vaccines against tumors. *Osteroff* teaches that epitope vaccines of hepatitis B and C viruses can be used to induce CD4 and CD8 T cell immunity to the viruses.

Therefore, a person skilled in the art would not have been led by the collective teachings of the cited prior art to make a composition comprising one or more OFA epitopes that specifically stimulate T cytotoxic lymphocytes, and which does not contain an OFA epitope that specifically stimulates T suppressor cells. Since neither *Fikes* nor *Osteroff* teaches or suggests anything about OFA epitopes, neither of these references supplies what is missing in *Rohrer* or *Irie*.

The Examiner also included claims 13-14 in the rejection. However, the Examiner has not provided any reason why these claims are rendered obvious by the cited references. Applicants respectfully submit that for the same reasons discussed above, these claims are not obvious over the cited references.

Therefore, Applicants respectfully submit that *Rohrer* or *Irie* in view of *Fikes* and *Osteroff* does not render the presently claimed invention (claims 1-24) obvious. The rejection of claims 1-13 under 35 U.S.C. § 103(a) should be withdrawn.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he/she telephone applicant's

attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: March 19, 2008

Respectfully submitted,

By Shawn P. Foley

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